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Stereocontrolled Construction of Seven-Membered Carbocycles Using a Combination of Brook Rearrangement-Mediated [3 + 4] Annulation and Epoxysilane Rearrangement

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Reactions of δ-silyl-γ,δ-epoxy-α,β-unsaturated acylsilane with alkenyl methyl ketone enolate afford highly functionalized cycloheptenone derivatives via a tandem sequence featuring the combination of Brook rearrangement-mediated [3 + 4] annulation and epoxysilane rearrangement. The reactions using an opposite combination of three and four carbon units, in which an epoxysilane moiety was incorporated in the four-carbon unit, also give satisfactory results. Also, the possibility of chirality transfer from epoxide to remote positions via the tandem sequence using an optically active epoxide has been demonstrated.

Introduction

Brook rearrangement-mediated[1] [3 + 4] annulation has been developed as a general approach for the synthesis of highly functionalized seven-membered[2] and eight-membered carbocycles[3] and oxygen heteroacycles.[4] The key of the annulation, which involves the reaction of acryloylsilanes **1** with enolates **2** of alkenyl alkyl ketones, is the stereospecific formation of a seven-membered ring **5** by an anionic oxy-Cope rearrangement of 1,2-divinylcyclopropanediolate intermediate **4** generated via Brook rearrangement of the 1,2-adduct **3** followed by intramolecular attack of the resultant carbanion at the carbonyl group (Scheme 1). From mechanistic studies[2c] of the annulation, we learned that the Cope rearrangement is a very rapid process even at lower temperatures, and consequently, the key of the annulation should be the formation of the 1,2-divinylcyclopro-

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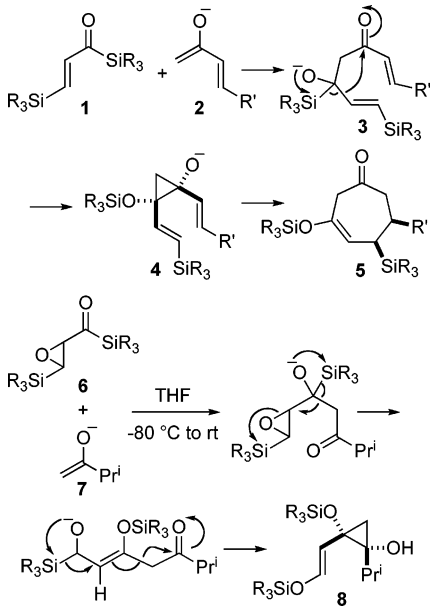
SCHEME 1



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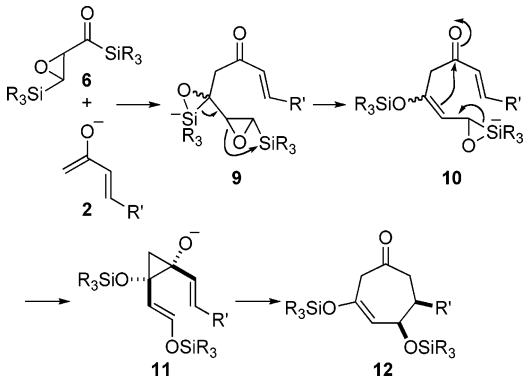


panediolate derivative **4**. On the other hand, we have recently reported[5b] that the reaction of *β*-silyl-α,*β*-epoxyacylsilane **6** with ketone enolate **7** affords vinylcyclopanediol derivative **8** via an epoxysilane rearrangement.[5]

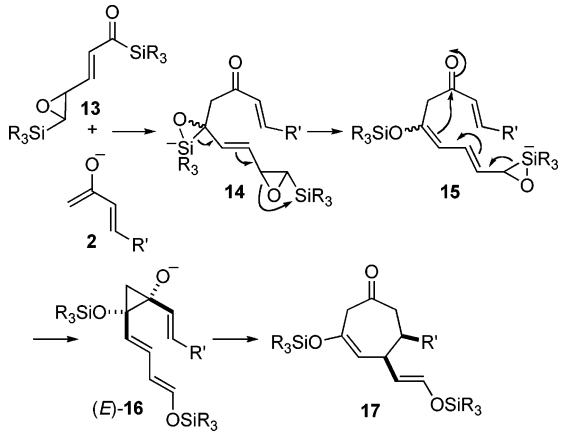
We conceived the idea that [3 + 4] annulation using **6** instead of acryloylsilane **1** as a three-carbon unit would afford highly functionalized cycloheptenone derivatives **12** via a tandem process that involves a 2-fold Brook rearrangement (**9** → **10** and **10** → **11**) as shown in Scheme 2. We also became interested in the possibility of remote chirality transfer from the epoxide to seven-membered rings by using homochiral epoxides, which is based on the results of our previous study,[5i] showing that the chirality of epoxide can be transferred to a carbanion via epoxysilane rearrangement and that the carbanion can participate in a [2,3]-Wittig rearrangement without racemization.

In this paper, we report a successful combination of Brook rearrangement-mediated [3 + 4] annulation and epoxysilane rearrangement as well as attempted chirality transfer through a tandem sequence.

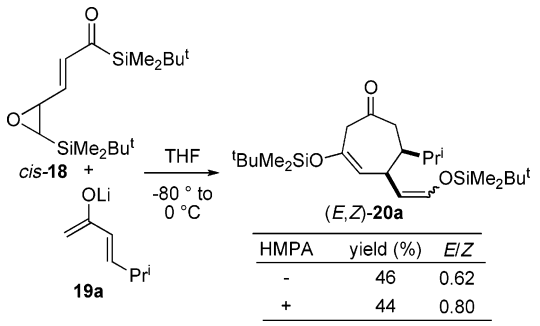
Results and Discussion

We first attempted to prepare **6** but could not obtain it in a good yield because of its tendency to undergo a silyl-migration reaction in the stage of epoxidation of the corresponding

SCHEME 3



SCHEME 4



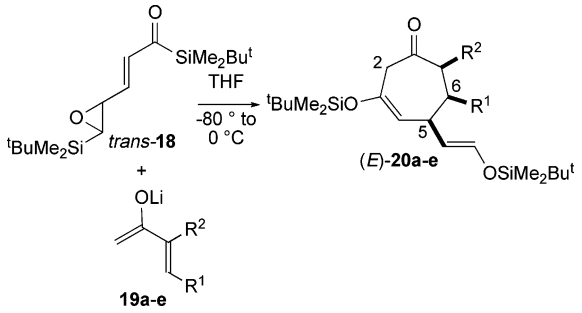
HMPA	yield (%)	*E*/*Z*
-	46	0.62
+	44	0.80

α-silylalcohol.[5b] We then focused on [3 + 4] annulation using the vinylogous derivative *trans*-**13**,[5e] which is outlined in Scheme 3. A carbanion generated by the first Brook rearrangement in **14** can induce a ring opening of the epoxide to give the second silicate intermediate **15**, which undergoes the second Brook rearrangement followed by an intramolecular attack to the carbonyl group to give the divinylcyclopropanediolate derivative (*E*)-**16**. We considered that the introduction of a double bond between an acylsilane moiety and a epoxysilane moiety would accelerate the anionic oxy-Cope rearrangement because of the sterically less congested nature and would offer more synthetic flexibility.

When lithium enolate **19a** of 5-methyl-3-hexen-2-one was added to a THF solution of *trans*-**18** at −80 °C and the mixture was allowed to warm to 0 °C, the expected [3 + 4] annulation product (*E*)-**20a** was isolated in 60% yield as a single diastereomer (Table 1, entry 1). The structure was assigned by spectral comparison with structurally related compounds.[2c] The stereochemistry was assigned on the basis of results of NOESY experiments that showed cross-peaks correlating to H-2, H-5, and H-6. Additional examples using **19b**−**e** are given in entries 2−5. Use of sodium or potassium enolate and of other solvents, including Et_2O and cyclopentyl methyl ether, and change in the order of the addition of reactants resulted in a decrease in yield.

The observed stereoselectivity, consistent with that expected on the basis of our previous work,[2c] can be explained by the concerted process of the anionic oxy-Cope rearrangement of divinylcyclopropanolate (*E*)-**16**. The formation of 5-(*Z*)-siloxyethenyl derivative was not detected. This prompted us to examine the reaction of the *cis*-epoxide derivative *cis*-**18**. When *cis*-**18** was reacted with **19a** under the same conditions as those employed for the trans counterpart, (*Z*)-**20a** was obtained as a

TABLE 1. Reaction of *trans*-18 with 19a−e



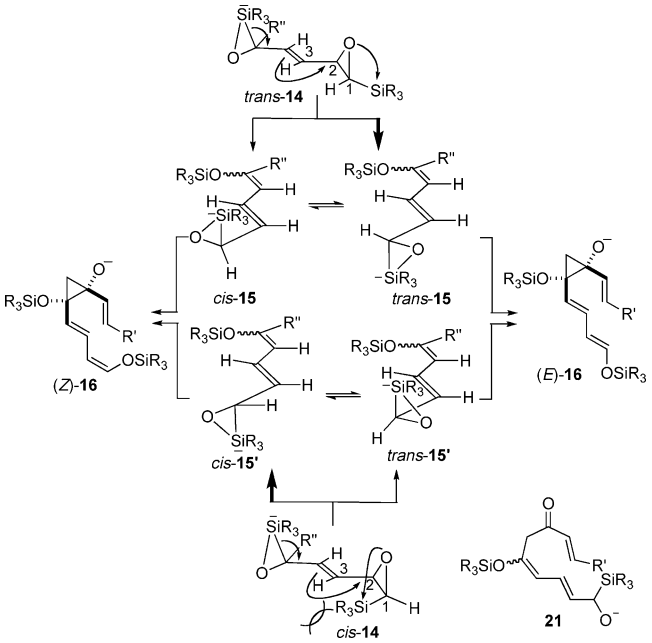
entry	compound	R^1	R^2	yield (%)
1	**19a**	$CHMe_2$	H	60
2	**19b**	$(CH_2)_4Me$	H	45
3	**19c**	OMe	H	38
4[a]	**19d**	Bn	H	31
5	**19e**	$(CH_2)_4$	$(CH_2)_4$	55

[a] HMPA (4 equiv) was added.

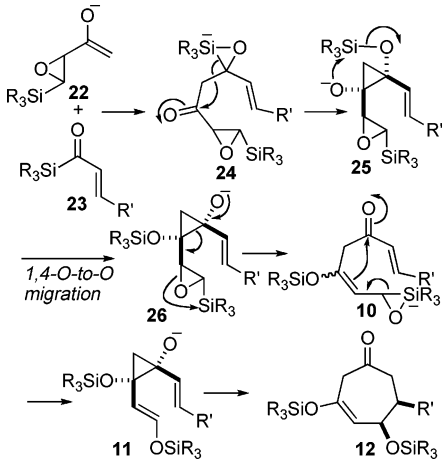
major isomer (E/Z = 0.62:1.0), which was not greatly affected by the addition of HMPA (Scheme 4).

For the observed selectivity, an explanation similar to that in the case of the reaction of **18** with a cyanide ion[5h] is applicable. The C−O bond cleavage of epoxide and Si−O bond formation in silicate intermediates *trans*-**14** and *cis*-**14**, generated from the addition of enolate to **18**, occur in a concerted fashion while keeping a parallel alignment (anti or syn) between the two bonds and the π-orbital to provide silicates *cis*- and *trans*-**15** and *cis*- and *trans*-**15′**, respectively (Scheme 5). Although both *cis*- and *trans*-**15** and *cis*- and *trans*-**15′** can be formed from both *trans*-**14** and *cis*-**14**, respectively, the processes, from *trans*-**14** to *trans*-**15** and from *cis*-**14** to *cis*-**15′**, leading to (*E*)-**16** and (*Z*)-**16**, respectively, seem to occur faster with rotation about the C1−C2 bond. The lower selectivity observed for the cis derivative may be explained by the eclipsing interaction between the hydrogen at C-3 and the *t*-butyldimethylsilyl group in the formation of silicate as shown. An alkoxide **21** is not

SCHEME 5



SCHEME 6



involved as an intermediate in the major pathway, or it is involved but was too short-lived to change its conformation.

Since it was found that both [3 + 4] annulation and epoxysilane rearrangement can be successfully connected, we next became interested in [3 + 4] annulation using the opposite combination of the three and four carbon units, **22** and **23**, in which an epoxysilane moiety was incorporated in the four-carbon unit as outlined in Scheme 6. The crucial step in the strategy, which features easier access to the four-carbon unit, is a 1,4-*O*-to-*O* migration of a silyl group in the cyclopropanediolate intermediate **25**, derived from adduct **24** via Brook rearrangement followed by attack of the generating carbanion to the carbonyl group, which allows the formation of **10**, exactly the same as that obtained from the normal version of [3 + 4] annulation, via a ring opening of the cyclopropane and the epoxide in **26** (Scheme 6). We previously observed similar silyl migration in the reaction of benzoyltrimethylsilane with methyl ketone enolates.[6]

When enolate *trans*-**27** was treated with acryloylsilane **23a**,[7] **28**, which can be formed via a ring opening of the cyclopropane and epoxide in the 1,4-*O*-to-*O* silyl migration product **29** followed by an intramolecular proton transfer in **30** before the second Brook rearrangement and then elimination of silanol in **31**, was obtained (Scheme 7). On the other hand, the reaction of *cis*-epoxide derivative *cis*-**27** resulted in the formation of **32**, which may arise from protonation of **33** (i.e., **34**, followed by ring opening of the resulting cyclopropanol and subsequent desilylation).[8] These results suggest that the cis isomer is reluctant to undergo the 1,4-*O*-to-*O* silyl migration presumably because of steric repulsion between the siloxy group and the epoxysilane moiety. In fact, quenching of the reaction at −60 °C allowed us to detect cyclopropanediol derivatives **34** (25%, diastereomeric mixture) and 1,2-adducts[9] as major products in addition to **35** (9%), **28** (7%), and **32** (6%).[10]

Since 1,4-*O*-to-*O* rearrangement followed by ring opening of the epoxide was found to occur in *trans*-epoxide *trans*-**27**

(6) Takeda, K.; Nakatani, J.; Nakamura, H.; Sako, K.; Yoshii, E.; Yamaguchi, K. *Synlett* **1993**, 841−843.

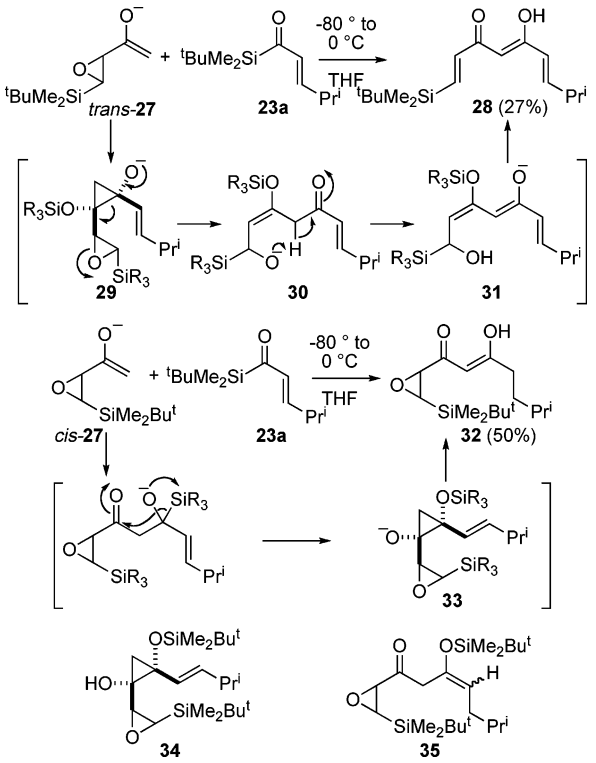
(7) Nowick, J. S.; Danheiser, R. L. *J. Org. Chem.* **1989**, *54*, 2798−2802.

(8) Takeda, K.; Yamawaki, K.; Hatakeyama, N. *J. Org. Chem.* **2002**, *67*, 1786−1794.

(9) ^{1}H NMR analysis of the crude reaction mixture suggested the presence of the 1,2-adduct, which could not be isolated due to decomposition during chromatographic purification.

(10) No product resulting from *O*-to-*O* migration was observed in the ^{1}H NMR of the crude reaction mixture.

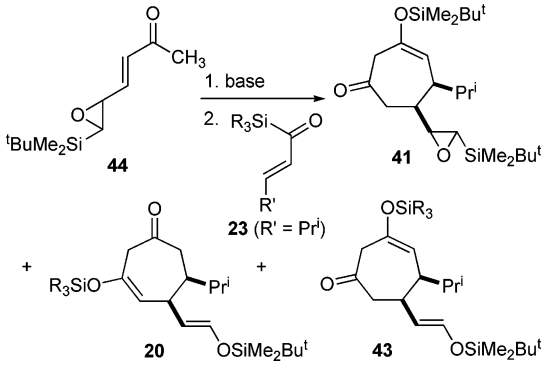
SCHEME 7



despite the failure of the overall process, we turned our attention to a vinylogous derivative **36** as a four-carbon unit, which cannot undergo intramolecular proton transfer and was prepared by a Wittig reaction. As shown in Scheme 8, annulation using **36** and **23** could, in principle, generate four types of divinylcyclopropanolates **38**, **39**, **16**, and **40** depending on the timing of the epoxysilane rearrangement and the 1,4-*O*-to-*O* silyl migration, which should provide seven-membered carbocycles **41**, **42**, **17**, and **43**, respectively, via an anionic oxy-Cope rearrangement.

When lithium enolate of **44** was treated with **23a** at −80 °C and allowed to warm to 0 °C, **41a** (a 1:1 diastereomeric mixture), an oxy-Cope rearrangement product of **38** before 1,4-*O*-to-*O* silyl migration, was obtained as a sole identifiable product in 50% yield (Table 2, entry 1). On the other hand, the use of sodium enolate (NaHMDS) resulted in the formation of desired cycloheptenone **20a** in 43% yield in addition to **41a** (16%) (Table 2, entry 2). Since this result can be interpreted as the consequence of acceleration of the 1,4-*O*-to-*O* silyl migration (**38** → **39**) by an increase in the ionic character of a counter cation, we examined the reaction using **23f** (R_3Si = $PhMe_2Si$) with the expectation of further acceleration of the 1,4-*O*-to-*O* silyl migration by introduction of a phenyl group to the silyl group.[5b,8,11,12] Treatment of sodium enolate of **44** with **23f** under the same conditions afforded **20f** in an improved 65% yield (Table 2, entry 3). Although the formation of **41f** could not be detected, instead **43f**, a 2-fold 1,4-*O*-to-*O* silyl migration product, was formed in 11% yield. These results show that the product distributions are a subtle balance among the relative

TABLE 2. Reaction of 23 with Enolate of 44



				yield (%)		
entry	compound	R_3Si	base	**41**	**20**	**43**
1[a]	**23a**	^{t}BuMe$_2$Si	LDA	50		
2	**23a**	^{t}BuMe$_2$Si	NaHMDS	16	43	
3	**23f**	$PhMe_2Si$	NaHMDS		65	11
4	**23g**	^{t}BuPh$_2$Si	NaHMDS		48	12

[a] HMPA was added.

rates of epoxysilane rearrangement, anionic oxy-Cope rearrangement, and 1,4-*O*-to-*O* silyl migration in **38** and **16**.[13]

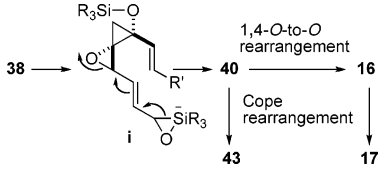
Having demonstrated that the combination of Brook rearrangement-mediated [3 + 4] annulation and epoxysilane rearrangement works well, we decided to attempt remote chirality transfer from an epoxide to a seven-membered ring by the use of enantiomerically enriched epoxysilanes. On the basis of the previous findings concerning the stereospecificity in the reactions of *trans*- and *cis*-**18** and on results of our recent study[5i] showing that the epoxide chirality can be transferred to a carbanion via Brook rearrangement and trapped intramolecularly almost without racemization by a [2,3]-Wittig rearrangement, we felt that it was worth examining the possibility of chirality transfer from an epoxide to a remote position.

We first conducted [3 + 4] annulation using enantiomerically enriched (−)-*trans*-**18** (90% ee) and **19a** under the same conditions as those employed for the racemic one to give **20a** with 15% ee. This result suggests that the epoxide chirality can be transferred to remote positions without complete racemization via an intramolecular process. One of the origins of the low enantioselectivity was thought to be partial racemization in **16** via ring opening−closure of the cyclopropane because we have observed that a ring opening and ring closing process is quite facile and competes with anionic oxy-Cope rearrangements.[2c] Therefore, we decided to verify this by the reaction of (−)-*trans*-**18** with lithium enolate of isopropyl methyl ketone, in which the anionic oxy-Cope rearrangement cannot occur. The

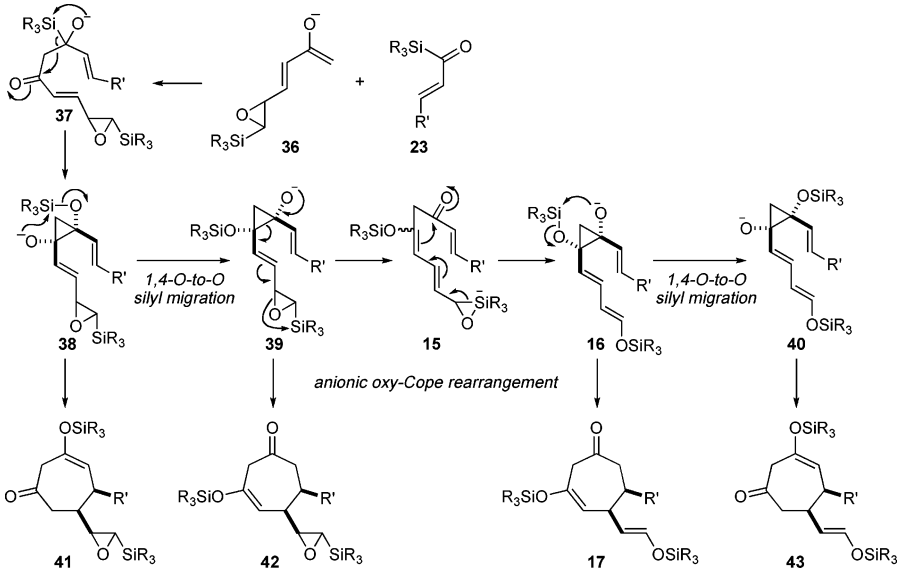
(11) Brook, A. G.; LeGrow, G. E.; MacRae, D. M. *Can. J. Chem.* **1967**, *45*, 239−253.

(12) Bräuer, N.; Michel, T.; Schaumann, E. *Tetrahedron* **1998**, *54*, 11481−11488.

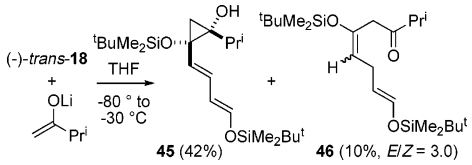
(13) A reviewer has suggested an alternative mechanism involving 1-oxaspiro[2.2]pentane intermediate **i** as a precursor for **17** and **43**. Although we cannot exclude this possibility, we feel this is unlikely in view of the fact that **43** was not detected in the reactions of *t*-butyldimethylsilyl derivativcs **23a**, **23h**, and **23i**, in which the rates of 1,4-*O*-to-*O* rearrangement in **40** is slower than those of dimethylphenylsilyl derivatives **23f** and **23j**.



SCHEME 8



SCHEME 9

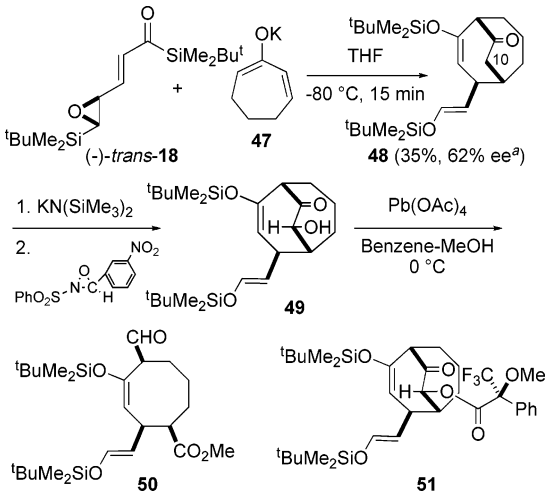


reaction resulted in complete racemization to give vinylcyclopropandiolate **45** in 42% yield together with uncyclized enol silyl ethers **46** (Scheme 9). This result suggests that the acceleration of anionic oxy-Cope rearrangement could suppress the racemization.

Our previous observation[3a] that the use of enolate of cycloalkenone in [3 + 4] annulation accelerates the anionic oxy-Cope rearrangement because of its fixed conformation, which is suitable for the rearrangement, prompted us to examine [3 + 4] annulation using an enolate of cycloalkenone. When (−)-*trans*-**18** was treated with potassium enolate **47** of 2-cycloheptenone, [3 + 4] annulation proceeded to give **48** in 35% yield with 62% ee (Scheme 10). As expected, the enantiomeric excess was greatly improved. The use of LDA or NaHMDS as a base resulted in a decrease in yield of **48**. The structure was assigned by spectral comparison with structurally related compounds[3a] and by ^{1}H NMR spectra showing an AB-type splitting pattern of the H-10 protons consisting of a pair of signals at δ 2.37 (1H, dd, J = 18.9, 4.1 Hz) and 2.81 (1H, br d, J = 18.9 Hz). Assignment of the absolute configuration of **48** was made by the modified Mosher method[14] after conversion into **51** via **49** (see Supporting Information). Transformation of **48** into a functionalized eight-membered carbocycle **50** could be achieved in a manner similar to that reported previously.[3a,4]

Next, we examined a relay of stereochemistry in [3 + 4] annulation using an opposite combination of the carbon units (Table 3). In the reaction of *t*-butyldimethylsilyl derivatives, the ee values were better than those obtained with the normal version of [3 + 4] annulation, the origin of which is not clear

SCHEME 10[a]



[a] Corrected for the ee of starting material (92% ee).

at present, in contrast to the fact that the ee values of phenyldimethysilyl and *t*-butyldiphenylsilyl derivatives were comparable.

The absolute stereochemistries of **20** and **43** were determined as follows (Scheme 11). *rac*-**20a** was transformed to bicyclic diol derivative **52** via a desilylation/reduction sequence. Separation of enantiomers of **52** was successfully carried out by using a preparative chiral HPLC column after conversion to *p*-bromobenzoates **53** and *ent*-**53**. Anomalous dispersions[15] in the determination of the structure by X-ray crystallography of **53** and comparison of the sign of specific rotations with that obtained from (−)-**44** established the absolute stereochemistry of **20a**. Derivatization of both **20j** and **43j** to **54j** allowed the determination of the absolute stereochemistry of **43j**.

Although it is difficult to speculate as to the origin of the observed stereoselection because of the complexity of the reaction cascade, there are several factors that appear to affect the stereoselection. First is the matter of diastereoselectivity in the formation of 1,2-adducts **55A** and **55B** or **56A** and **56B**, in

(14) (a) Ohtani, I.; Kusumi, T.; Kashman, Y.; Kakisawa, H. *J. Am. Chem. Soc.* **1991**, *113*, 4092−4096. (b) Kusumi, T. *J. Synth. Org. Chem. Jpn.* **1993**, *51*, 462−470.

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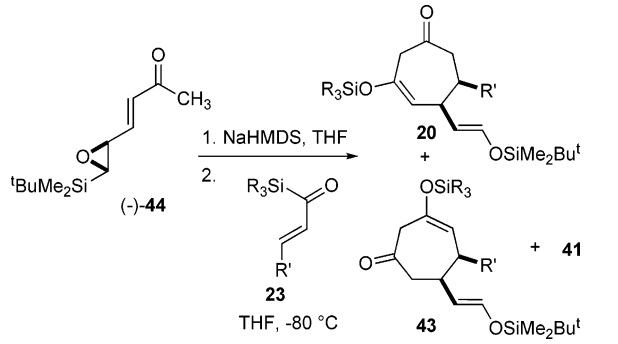
TABLE 3. Reaction of 23 with Enolate of (−)-44



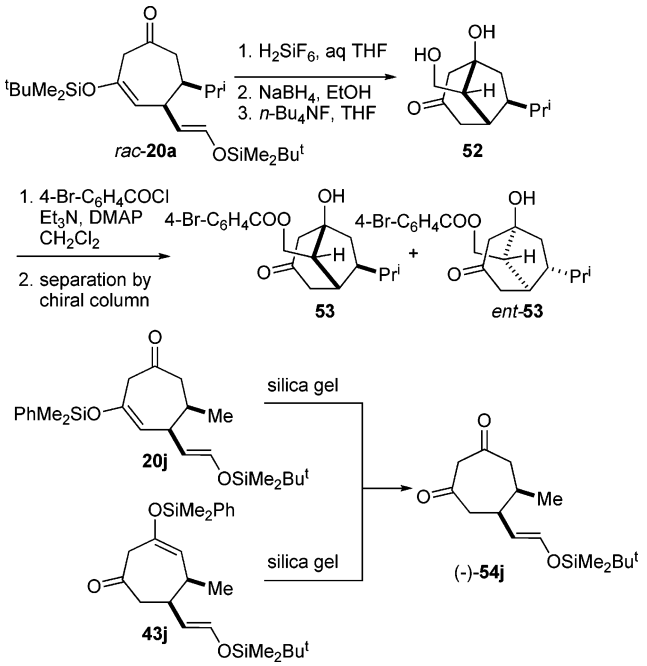
			20		43		41
compound	R′	R_3Si	yield (%)	ee (%)[a]	yield (%)	ee (%)[a]	yield (%)
23a	*i*-Pr	^{t}BuMe$_2$Si	43	37			16
23h	Et	^{t}BuMe$_2$Si	29	33			16
23i	Cy	^{t}BuMe$_2$Si	36	25			4
23j	Me	PhMe$_2$Si	70	12	8	17	
23f	*i*-Pr	PhMe$_2$Si	65	17	11	14	
23g	*i*-Pr	^{t}BuPh$_2$Si	48	15	12	16	

[a] Corrected for the ee of the starting material (89% ee).

which good selectivity does not seem to be expected. Our previous study[2c] has shown that there exists a fast equilibrium between a 1,2-adduct and an enolate anion at −80 °C in reactions of acryloylsilanes with ketone enolates (Scheme 12). Therefore, if the diastereomeric 1,2-adducts **55A** and **55B**, interconvertible via the equilibrium, have a different reactivity toward Brook rearrangement in **56A** and **56B** followed by a ring opening of epoxide, either isomer **55A** or **55B** can be transformed to the next intermediate faster than the other.

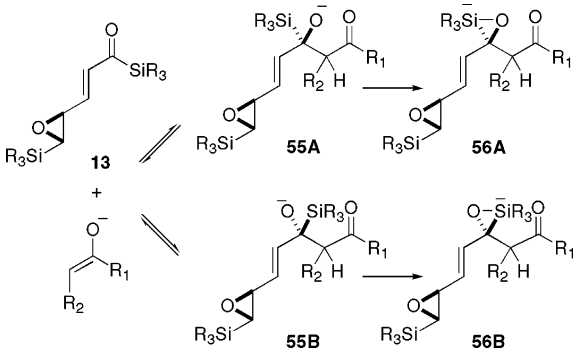
The next step is the formation of the second silicate intermediate (*Z*)-**57** or (*E*)-**57** via first a Brook rearrangement and a ring opening of the epoxide. Assuming that the tandem

SCHEME 11[a]

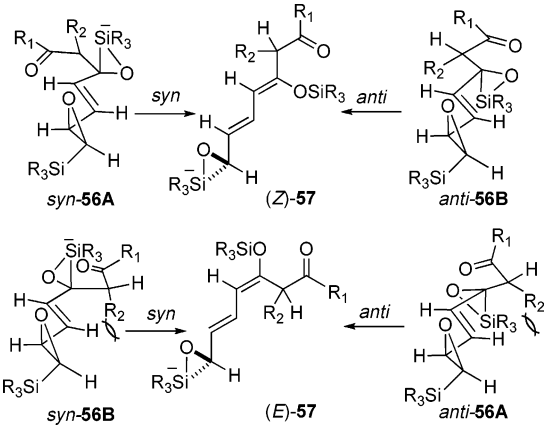


[a] For details, see the Supporting Information

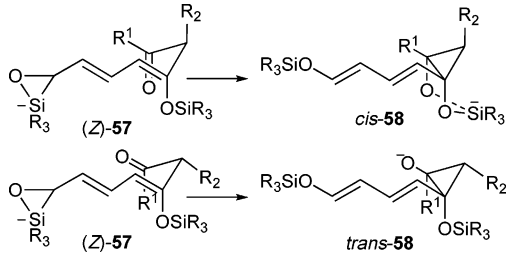
SCHEME 12



SCHEME 13



SCHEME 14

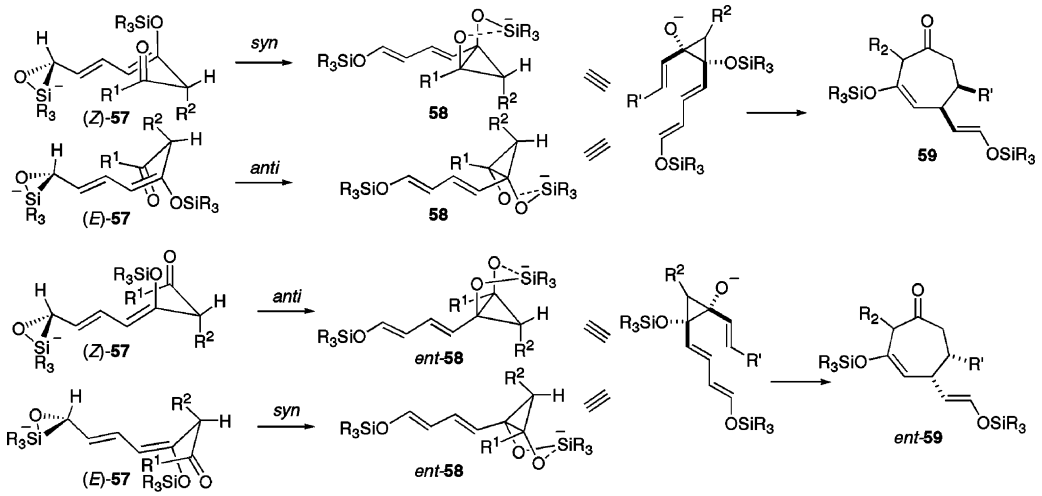


sequence takes place on the conformations, in which the C−Si bond, π-orbitals of the double bond, and cleaving the C−O bond of the epoxide adopt an almost parallel orientation,[16] (*Z*)-silicate (*Z*)-**57** can be formed from *syn*-**56A** or *anti*-**56B** and (*E*)-silicate (*E*)-**57** can be formed from *syn*-**56B** or *anti*-**56A** as shown Scheme 13. In the intermediates *syn*-**56B** and *anti*-**56A**, an allylic strain, as shown, develops, whereas this type of interaction is absent in the intermediates *syn*-**56A** and *anti*-**56B**. Consequently, the ratio of (*Z*)-**57**/(*E*)-**57** should reflect the difference in the interaction.

When one considers the stereoselectivity in the transformation of (*Z*)-**57** and (*E*)-**57** to divinylcyclopropanolates **58**, two issues are addressed. First is the matter of the facial selectivity in the formation of cyclopropanediolates by nucleophilic attack on the ketone carbonyl. Our previous studies[8] on the formation of cyclopropanediolates by internal carbonyl attack of an α-siloxy carbanion have shown that the formation of *cis*-diolate derivative *cis*-**58** predominates because of the internally O−Si coordinated structure (examples on (*Z*)-**57** shown in Scheme 14).

Second is the facial selectivity of the dienylsilicate portion in the cyclopropane formation, concerning the relative arrange-

SCHEME 15



ment (syn/anti) of the cleaving C−Si bond and the newly forming C−C bond. Assuming that the same stereoelectronic preferences as those in the formation of **57** can apply to this case, (*Z*)-**57** and (*E*)-**57** give divinylcyclopropanolate **58** in a syn and an anti fashion, and they give *ent*-**58** in an anti and a syn fashion, respectively (Scheme 15).

According to our hypothesis, the fact that **59** was formed as a major enantiomer and the fact that the use of cyclic ketone enolate **47** (R^2 is an alkyl group), in which a more severe allylic strain can be created, gave better enantioselectivity than those observed for methyl ketone enolate suggest that its immediate precursor is **58**, which should be derived from (*Z*)-**57** in syn-type addition.

The lower ee values observed in the reactions of phenyldimethlsilyl derivatives **23j** and **23f** and *t*-butyldiphenylsilyl derivative **23g** in comparison with those of *t*-butyldimethylsilyl derivatives **23a**, **23h**, and **23i** (Table 3) can be explained as a result of incomplete equilibration between **37** or **38** and the starting materials owing to acceleration of the first 1,4-*O*-to-*O* migration of the silyl group by introduction of a phenyl group on the silyl group.

In summary, we have demonstrated that two tandem reactions, Brook rearrangement-mediated [3 + 4] annulation and epoxysilane rearrangement, both of which we have developed, have been successfully combined to provide a new methodology for the construction of seven- and eight-membered carbocycles. Furthermore, the present study that involves a chirality transfer of epoxide to the remote positions via formal chiral carbanions has provided some new aspects of asymmetric synthesis.

(16) To the best of our knowledge, there is no precedent for a stereochemical discussion concerning Brook rearrangement in α-silyl allylalkoxides. For the Brook rearrangement in α-oxidosilanes with a *β*-leaving group, see: (a) Vedejs, E.; Arnost, M. J.; Eustache, J. M.; Krafft, G. A. *J. Org. Chem.* **1982**, *47*, 4384−4386. (b) Hudrlik, P. F.; Hudrlik, A. M.; Kulkarni, A. K. *J. Am. Chem. Soc.* **1985**, *107*, 4260−4264. (c) Reich, H. J.; Holtan, R. C.; Bolm, C. *J. Am. Chem. Soc.* **1990**, *112*, 5609−5617. (d) Nakajima, T.; Segi, M.; Sugimoto, F.; Hioki, R.; Yokota, S.; Miyashita, Y. *Tetrahedron* **1993**, *49*, 8343−8358. (e) Jin, F.; Xu, Y.; Huang, W. *J. Chem. Soc., Perkin Trans. 1* **1993**, 795−799. (f) Brigaud, T.; Doussot, P.; Portella, C. *J. Chem. Soc., Chem. Commun.* **1994**, 2117−2118. (g) Lefebvre, O.; Brigaud, T.; Portella, C. *Tetrahedron* **1998**, *54*, 5939−5948. (h) Lefebvre, O.; Brigaud, T.; Portella, C. *Tetrahedron* **1999**, *55*, 7233−7242. (i) Fleming, I.; Roberts, R. S.; Smith, S. C. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1215−1228.

Experimental Section

General Procedure A for [3 + 4] Annulation Using 18 and 19: Reaction of *trans*-18 with Lithium Enolate of 5-Methyl-3-hexene-2-one (19a). To a cooled (−80 °C) solution of lithium diisopropylamide (LDA), prepared from diisopropylamine (104 *μ*L, 0.742 mmol) and *n*-BuLi (2.36 M in hexane, 316 *μ*L, 0.746 mmol) in THF (0.4 mL), was added dropwise a solution of 5-methyl-3-hexene-2-one (98 mg, 0.746 mmol) in THF (0.8 mL). After being stirred at −80 °C for 25 min, the solution was added dropwise via cannula to a cooled (−80 °C) solution of *trans*-**18** (203 mg, 0.621 mmol) in THF (30 mL). The reaction mixture was allowed to warm to 0 °C over a period of 20 min and then quenched by 10% aqueous NH_4Cl solution (30 mL). The mixture was separated, and the aqueous phase was extracted with Et_2O (10 mL × 2). Combined organic phases were washed with saturated brine (30 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 10 g; elution with hexane/Et_2O = 25:1) to give (*E*)-**20a** (165 mg, 60%). Colorless oil. R_f = 0.33 (hexane/Et_2O = 10:1). IR (film) 1712, 1651, 1470, 1255, 1171 cm^{-1}. ^1H NMR (400 MHz, C_6D_6) *δ* 0.16, 0.16, 0.17, and 0.20 (each 3H, s, Si*Me*$_2$), 0.74 and 0.81 (each 3H, d, *J* = 6.6 Hz, CH*Me*$_2$), 0.99 (18 H, s, *t*-Bu), 1.49 (1H, d-sep, *J* = 6.6, 6.6 Hz, C*H*Me$_2$), 1.78−1.85 (1H, m, H-6), 2.25 (1H, dd, *J* = 15.4, 4.4 Hz, H-7), 2.43 (1H, dd, *J* = 15.4, 12.2 Hz, H-7), 2.89 (1H, d, *J* = 15.6 Hz, H-2), 3.07−3.11 (1H, m, H-5), 3.48 (1H, dm, *J* = 15.6 Hz, H-2), 5.04 (1H, dd, *J* = 6.8, 2.4 Hz, H-4), 5.16 (1H, dd, *J* = 12.0, 8.3 Hz, H-1′), 6.34 (1H, d, *J* = 12.0 Hz, H-2′). ^{13}C NMR (100 MHz, C_6D_6) *δ* −5.1, −5.1, −4.3, and −4.3 (Si*Me*$_2$), 18.1 and 18.4 (*C*Me$_3$), 20.4 and 21.3 (*CHMe*$_2$), 25.8 and 25.8 (C*Me*$_3$), 29.9 (*C*HMe$_2$), 37.2 (C-5), 44.4 (C-7), 45.0 (C-6), 49.3 (C-2), 109.8 (C-1′), 112.4 (C-4), 142.6 (C-2′), 145.3 (C-3), 205.4 (C-1). HRMS calcd for $C_{24}H_{46}O_3Si_2$ 438.2985, found 438.2947. The relative stereochemistry at C-5 and C-6 was assigned on the basis of NOESY correlation among the hydrogens at C-2, C-5, and C-6.

Reaction of 23a with *trans*-27. To a cooled (−80 °C) solution of KHMDS (0.61 M in THF, 3.0 mL, 1.83 mmol) in THF (670 *μ*L) was added dropwise a solution of (3*R**,4*R**)-4-(*tert*-butyldimethylsilyl)-3,4-epoxybutan-2-one (368 mg, 1.84 mmol) in THF (1.8 mL), and then the solution was stirred at the same temperature for 20 min. To this solution was added dropwise a cooled (−80 °C) solution of **23a** (300 mg, 1.41 mmol) in THF (26 mL) over a period of 16 min, and the reaction mixture was allowed to warm to 0 °C over a period of 30 min. The solution was diluted with 10% aqueous NH_4Cl solution (15 mL), phases were separated, and the aqueous phase was extracted with Et_2O (10 mL × 2). Combined organic phases were washed with saturated brine (30 mL), dried, and concentrated. The residual oil was subjected to column chroma-

tography (silica gel, 50 g, elution with hexane/Et_2O = 50:1) to give **28** (107 mg, 27%). Colorless oil. R_f = 0.22 (hexane/CH_2Cl_2 = 3:1). IR (film) 1645, 1621, 1564, 1465, 1254 cm^{-1}. ^1H NMR (500 MHz) δ 0.10 (6H, s, Si*Me*$_2$), 0.90 (9H, s, *t*-Bu), 1.08 (3H, d, J = 6.6 Hz, H-9), 2.49 (1H, dd-sep, d, J = 6.9, 6.6, 1.4 Hz, H-8), 5.67 (1H, s, H-4), 5.95 (1H, dd, J = 15.8, 1.4 Hz, H-6), 6.38 (1H, d, J = 18.8 Hz, H-2), 6.88 (1H, dd, J = 15.8, 6.9 Hz, H-7), 7.14 (1H, d, J = 18.8 Hz, H-1). ^{13}C NMR (125 MHz) δ −6.2 (Si*Me*$_2$), 16.9 (*C*Me$_3$), 21.6 (C-9), 26.6 (C*Me*$_3$), 31.5 (C-8), 99. 7 (C-4), 125.1 (C-6),-141.0 (C-2), 142.1 (C-1), 152.2 (C-7), 180.5, and 186.7 (C-3 and C-5). HRMS calcd for $C_{16}H_{28}O_2Si$ 280.1859, found 280.1857.

General Procedure B for [3 + 4] Annulation Using 23 and 44: Reaction of 23f with Sodium Enolate of 44. To a cooled (−80 °C) solution of NaHMDS (1.06 M in THF, 422 μL, 0.448 mmol) in THF (473 μL) was added dropwise a solution of **44** (101 mg, 0.448 mmol) in THF (895 μL), and then the solution was stirred at the same temperature for 25 min. To this solution was added dropwise a cooled (−80 °C) solution of **23f** (80 mg, 0.344 mmol) in THF (5.1 mL) over a period of 5 min, and the solution was stirred at the same temperature for 7 min before addition of AcOH (1 M in THF, 448 μL). The resulting mixture was diluted with 10% aqueous NH_4Cl solution (20 mL), phases were separated, and the aqueous phase was extracted with Et_2O (5 mL × 2). Combined organic phases were washed with saturated brine (30 mL), dried, and concentrated. The residual oil was subjected to column chromatography (florisil, 4 g, elution with hexane/Et_2O = 4:1) to give a mixture of **20f** and **43f**. This mixture was separated by MPLC (elution with hexane/Et_2O/CH_2Cl_2 = 20:1:1) to give **20f** (102 mg, 65%) and **43f** (16 mg, 11%). **20f**: Colorless oil. R_f = 0.42 (hexane/Et_2O = 5:1). IR (film) 1712, 1426, 1654, 1257 cm^{-1}. ^1H NMR (500 MHz) δ 0.11 and 0.11 (each 3H, s, Si*Me*$_2$Bu^t), 0.45 and 0.46 (each 3H, s, Si*Me*$_2$Ph), 0.85 and 0.91 (each 3H, d, J = 6.6 Hz, CH*Me*$_2$), 0.90 (9H, s, *t*-Bu), 1.63 (1H, d-sep, J = 6.6, 6.6 Hz, C*H*Me$_2$), 1.91 (1H, dddd, J = 11.7, 6.6, 4.8, 3.0 Hz, H-6), 2.37-(1H, dd, J = 14.7, 4.8 Hz, H-7), 2.44 (1H, dd, J = 14.7 Hz, 11.7, H-7), 2.84 (1H, d, J = 16.3 Hz, H-2), 2.99 (1H, ddd, J = 8.2, 6.9, 3.0 Hz, H-5), 3.58 (1H, ddd, J = 16.3, 2.1, 2.1 Hz, H-2), 4.84 (1H, dd, J = 6.9, 2.5 Hz, H-4), 4.86 (1H, dd, J = 11.9, 8.2 Hz, H-1′), 6.11 (1H, d, J = 11.9 Hz, H-2′), 7.34−7.43 (3H, m, Ph), 7.55−7.59 (2H, m, Ph). ^{13}C NMR (125 MHz) δ −5.0 (Si*Me*$_2$Bu^t), −1.0 and −1.0 (Si*Me*$_2$Ph), 18.5 (*C*Me$_3$), 20.1 and 21.5 (CH*Me*$_2$), 25.9 (C*Me*$_3$), 29.5 (*C*HMe$_2$), 36.9 (C-5), 43.5 (C-7), 46.0 (C-6), 49.5 (C-2), 109.9 (C-1′), 112.8 (C-4), 128.1, 130.1, 133.5, 137.3 (Ph), 142.2 (C-2′), 144.5 (C-3), 208.6 (C-1). HRMS calcd for $C_{26}H_{42}O_3Si_2$ 458.2672, found 458.2682. **43f**: Colorless oil. R_f = 0.42 (hexane/Et_2O = 5:1). IR (film) 1712, 1657, 1257 cm^{-1}. ^1H NMR (500 MHz) δ 0.11 (6H, s, Si*Me*$_2$Bu^t), 0.49 and 0.50 (each 3H, s, Si*Me*$_2$Ph), 0.73 and 0.77 (each 3H, d, J = 6.4 Hz, CH*Me*$_2$), 0.91 (9H, s, *t*-Bu), 1.37 (1H, d-sep, J = 10.3, 6.4 Hz, C*H*Me$_2$), 1.67 (1H, ddd, J = 10.3, 7.3, 4.4 Hz, H-5), 2.22 (1H, dd, J = 10.3, 7.6 Hz, H-7), 2.60 (1H, dd, J = 10.8, 10.3 Hz, H-7), 2.74 (1H, dddd, J = 10.8, 10.5, 7.3, 4.4 Hz, H-6), 2.77 (1H, d, J = 19.7 Hz, H-2), 3.30 (1H, d, J = 19.7 Hz, H-2), 4.70 (1H, dd, J = 7.3, 2.3 Hz, H-4), 4.73 (1H, dd, J = 11.9, 10.5 Hz, H-1′), 6.23 (1H, d, J = 11.9 Hz, H-2′), 7.36−7.43 (3H, m, Ph), 7.57−7.62 (2H, m, Ph). ^{13}C NMR (125 MHz) δ −5.1 (Si*Me*$_2$Bu^t), −1.1 and −1.0 (Si*Me*$_2$-Ph), 18.5 (*C*Me), 20.0 and 21.9 (CH*Me*$_2$), 25.9 (C*Me*$_3$), 30.2 (*C*HMe$_2$), 41.7 (C-6), 45.5 (C-5), 48.4 (C-7), 50.8 (C-2), 110.6 and 110.7 (C-4 and C-1′), 128.2, 130.2, 133.6, 137.0 (Ph), 141.6 (C-2′), 147.6 (C-3), 210.1 (C-1). HRMS calcd for $C_{26}H_{42}O_3Si_2$ 458.2672, found 458.2678.

Reaction of (−)-*trans*-18 with Lithium Enolate of 3-Methyl-2-butanone. To a cooled (−80 °C) solution of lithium diisopropylamide (LDA) prepared from diisopropylamine (82 μL, 0.584 mmol) and *n*-BuLi (2.25 M in hexane, 248 μL, 0.559 mmol) in THF (0.3 mL) was added dropwise a solution of 3-methyl-2-butanone (48 mg, 0.569 mmol) in THF (0.6 mL). After being stirred at −80 °C for 15 min, the solution was added dropwise to a cooled (−80 °C) solution of (−)-*trans*-**18** (166 mg, 0.508 mmol) in THF (30 mL). The reaction mixture was allowed to warm to −30 °C over a period of 15 min and then quenched with 10% aqueous NH_4-Cl solution (30 mL). The mixture was separated, and the aqueous phase was extracted with Et_2O (10 mL × 2). Combined organic phases were washed with saturated brine (40 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 15 g; elution with hexane/Et_2O = 30:1) to give **45** (88 mg, 42%) and an inseparable mixture of (*E*)- and (*Z*)-**46** (22 mg, 10%, *E*/*Z* = 3.0). Compound **45** was determined to be racemic using a Daicel Chiralcel OD−H column (4.6 mm × 250 mm): flow rate 0.5 mL/min, 254 nm, eluent hexane, t_R = 7.7 min, 8.2 min. **45**: Colorless oil. R_f = 0.52 (hexane/Et_2O = 5:1). IR (film) 3519, 1706, 1654, 1620, 1469, 1256 cm^{-1}. ^1H NMR (500 MHz) δ 0.09 and 0.11 (each 3H, s, Si*Me*$_2$), 0.16 (6H, s, Si*Me*$_2$), 0.67 (1H, d, J = 7.1 Hz, H-3), 0.85−0.95 (4H, m, H-3 and CH*Me*$_2$), 0.88 and 0.92 (each 9H, s, *t*-Bu), 1.06 (3H, d, J = 6.9 Hz, CH*Me*$_2$), 1.18 (1H, sep, J = 6.9 Hz, C*H*Me$_2$), 2.90 (1H, s, OH), 5.55 (1H, d, J = 15.1 Hz, H-1′), 5.72 (1H, dd, J = 11.7, 11.0 Hz, H-3′), 5.93 (1H, dd, J = 15.1, 11.0 Hz, H-2′), 6.52 (1H, d, J = 11.7 Hz, H-4′). ^{13}C NMR (100 MHz) δ −5.1, −5.1, −3.8, and −3.0 (Si*Me*$_2$), 18.0 and 18.3 (CH*Me*$_2$), 18.1 and 18.4 (*C*Me$_3$), 24.5 (C-3), 25.8 and 26.0 (C*Me*$_3$), 31.6 (*C*HMe$_2$), 62.7 and 64.4 (C-1, C-2), 112.9 (C-3′), 126.5 (C-1′), 127.3 (C-2′), 144.8 (C-4′). HRMS calcd for $C_{22}H_{43}O_3Si_2$ (M^+ − H) 411.2751, found 411.2750. The relative stereochemistry at C-1 and C-2 was assigned on the basis of the observed correlation between the hydrogens at C-1′ and C*H*Me$_2$ in NOESY experiments. **46**: (*E*/*Z* mixture) Colorless oil. R_f = 0.48 (hexane/Et_2O = 5:1). IR (film) 1717, 1658, 1586, 1468, 1255 cm^{-1}. HRMS calcd for $C_{22}H_{44}O_3Si_2$ 412.2829, found 412.2823. ^1H NMR (500 MHz) signals assigned to (*E*)-**46** in the mixture of (*E*)- and (*Z*)-46. δ 0.12 and 0.14 (each 6H, s, Si*Me*$_2$), 0.88 and 0.91 (each 9H, s, *t*-Bu), 1.08 (6H, d, J = 7.1 Hz, H-1), 2.55 (2H, dd, J = 7.6, 6.6 Hz, H-7), 2.78 (1H, sep, J = 7.1 Hz, H-2), 3.19 (2H, s, H-4), 4.72 (1H, t, J = 7.6 Hz, H-6), 4.95 (1H, dt, J = 11.9, 6.6 Hz, H-8), 6.24 (1H, d, J = 11.9 Hz, H-9). ^{13}C NMR (125 MHz) signals assigned to (*E*)-**46** in the mixture of (*E*)- and (*Z*)-**46**. δ −5.1, −4.4 (Si*Me*$_2$), 18.1 and 18.7 (*C*Me$_3$), 18.5 (C-1), 25.5 (C-7), 25.8 and 25.9 (C*Me*$_3$), 39.5 (C-2), 44.6 (C-4), 108.7 (C-6), 110.2 (C-8), 140.9 (C-9), 146.1 (C-5), 211.1 (C-3). ^1H NMR (500 MHz) signals assigned to (*Z*)-**46** in the mixture of (*E*)- and (*Z*)-**46**. δ 0.12 and 0.14 (each 6H, s, Si*Me*$_2$), 0.91 and 0.92 (each 9H, s, *t*-Bu), 1.35 (6H, d, J = 6.9 Hz, H-1), 2.64 (2H, dd, J = 7.1, 6.6 Hz, H-7), 2.86 (1H, sep, J = 6.9 Hz, H-2), 3.10 (2H, s, H-4), 4.53 (1H, t, J = 7.1 Hz, H-6), 4.95 (1H, dt, J = 11.9, 6.6 Hz, H-8), 6.24 (1H, d, J = 11.9 Hz, H-9). ^{13}C NMR (125 MHz) signals assigned to (*Z*)-**46** in the mixture of (*E*)- and (*Z*)-**46**. δ −5.1, −3.8 (Si*Me*$_2$), 18.4 and 18.7 (*C*Me$_3$), 18.5 (C-1), 23.8 (C-7), 25.8 and 25.9 (C*Me*$_3$), 38.9 (C-2), 49.8 (C-4), 110.0 (C-8), 112.0 (C-6), 140.8 (C-9), 144.5 (C-5), 211.9 (C-3). The enol silyl ether geometries were determined on the basis of NOESY experiments.

(1*S*,4*S*,5*S*)-2-(*tert*-Butyldimethylsilyloxy)-4-((*E*)-2-(*tert*-butyldimethylsilyloxy)vinyl)bicyclo[3.3.2]dec-2-en-9-one (48). To a cooled (−80 °C) solution of KHMDS (0.51 M in toluene, 1.44 mL, 0.735 mmol) in THF (397 μL) was added dropwise a solution of 2-cycloheptenone (81 mg, 0.735 mmol) in THF (735 μL) over a period of 2 min, and then the solution was stirred at the same temperature for 30 min. To this solution was added dropwise a cooled (−80 °C) solution of (−)-*trans*-**18** (200 mg, 0.612 mmol) in THF (10.8 mL) over a period of 12 min. After stirring at −80 °C for 5 min, the reaction mixture was quenched by addition of AcOH (1 M in THF, 735 μL). The resulting mixture was diluted with 10% aqueous NH_4Cl solution (20 mL), phases were separated, and the aqueous phase was extracted with Et_2O (5 mL × 2). Combined organic phases were washed with saturated brine (20 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 11 g, elution with hexane/Et_2O = 22:1) to give **48** (93 mg, 35%). Colorless oil. R_f = 0.37 (hexane/Et_2O = 6:1). $[\alpha]^{28}_D$ +1.6 (*c* 1.0, $CHCl_3$). The optical purity was determined to be 62% ee using a Daicel Chiralcel OD−H

column (4.6 mm × 250 mm): eluent hexane, flow rate 0.5 mL/min, UV detection at 205 nm, t_R = 15.6 min (minor), 19.2 min (major). IR (film) 1704, 1657, 1620, 1468, 1255 cm^{-1}. ^1H NMR (500 MHz) δ 0.13 (12H, s, Si*Me*$_2$), 0.90 and 0.91 (each 9H, s, *t*-Bu), 1.46 (1H, dddd, J = 13.7, 13.7, 3.7, 3.7 Hz, H-6), 1.51 (1H, dddd, J = 13.7, 13.7, 3.7, 3.7 Hz, H-8), 1.68 (1H, br ddd, J = 13.7, 3.7, 3.7 Hz, H-7), 1.85 (1H, ddddd, J = 13.7, 13.7, 13.7, 3.7, 3.7 Hz, H-7), 1.93−2.05 (3H, m, H-8, H-6 and H-5), 2.37 (1H, dd, J = 18.9, 4.1 Hz, H-10), 2.81 (1H, br d, J = 18.9 Hz, H-10), 2.91−2.97 (1H, br m, H-4), 3.15 (1H, d, J = 6.9 Hz, H-1), 5.02 (1H, d, J = 5.3 Hz, H-3), 5.03 (1H, dd, J = 12.1, 7.3 Hz, H-1′), 6.27 (1H, dd, J = 12.1, 1.1 Hz, H-2′). ^{13}C NMR (125 MHz) δ −5.0, −5.0, −4.3 and −4.1 (Si*Me*$_2$), 18.1 and 18.6 (*C*Me$_3$), 22.3 (C-7), 25.8 and 25.9 (C*Me*$_3$), 28.5 (C-8), 34.4, 34.8 (C-5 and C-6), 39.4 (C-4), 43.1 (C-10), 61.6 (C-5), 112.9 (C-3), 115.2 (C-1′), 141.5 (C-2′), 145.4 (C-2), 211.9 (C-9). HRMS calcd for $C_{24}H_{44}O_3Si_2$ 436.2829, found 436.2808.

Methyl (1*R,4*R**,5*S**)-2-(*tert*-Butyldimethylsilyloxy)-4-((*E*)-2-(*tert*-butyldimethylsilyloxy)vinyl)-5-formylcyclooct-2-enecarboxylate (50).** To a cooled (ice water) solution of **49** (140 mg, 0.289 mmol) in MeOH-benzene (1:1, 14.4 mL) was added $Pb(OAc)_4$ (80%, 188 mg, 0.347 mmol), and the mixture was stirred at the same temperature for 15 min before dilution with hexane (14 mL). The reaction mixture was filtered through a pad of silica gel, and the filtrate was concentrated. The residual oil was diluted with Et_2O (5 mL) and poured into saturated aqueous $NaHCO_3$ solution (10 mL). Phases were separated, and the aqueous phase was extracted with Et_2O (5 mL × 2). Combined organic phases were washed with saturated brine (10 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel 8 g, elution with hexane/Et_2O = 5:1) to give **50** (130 mg, 93%). Colorless needles (hexane-Et_2O); mp 103−104 °C, R_f = 0.52 (hexane/Et_2O = 2:1). IR (KBr) 1744, 1653, 1620, 1308, 1256 cm^{-1}. ^1H NMR (500 MHz, C_6D_6) δ 0.11, 0.12, 0.19, 0.21 (each 3H, s, Si*Me*$_2$), 0.96 and 0.98 (each 9H, s, *t*-Bu), 1.11−1.21 (1H, m, H-7), 1.20 (1H, dddm, J = 14.9, 9.6, 4.4 Hz, H-6), 1.48 (1H, ddddm, J = 14.4, 9.4, 9.2, 3.7 Hz, H-7), 1.70 (1H, dddm, J = 14.9, 9.2, 8.7 Hz, H-6), 1.86 (1H, dddd, J = 14.2, 9.4, 3.9, 3.7 Hz, H-8), 2.01 (1H, dddd, J = 14.2, 12.4, 7.6, 3.7 Hz, H-8), 2.24 (1H, dddd, J = 8.7, 4.4, 3.9, 0.9 Hz, H-5), 3.03 (1H, dddd, J = 9.4, 7.1, 3.9, 1.1 Hz, H-4), 3.39 (1H, dd, J = 12.4, 3.9 Hz, H-1), 3.47 (3H, s, CO_2*Me*), 4.98 (1H, d, J = 9.4 Hz, H-3), 5.50 (1H, dd, J = 12.1, 7.1 Hz, H-1′), 6.47 (1H, dd, J = 12.1, 1.1 Hz, H-2′), 9.53 (CHO). ^{13}C NMR (125 MHz, C_6D_6) δ −5.2, −4.8, and −4.4 (Si*Me*$_2$), 18.1 and 18.4 (*C*Me$_3$), 22.5 (C-7), 25.6 and 25.8 (C*Me*$_3$), 26.6 (C-6), 31.1 (C-8), 37.2 (C-4), 46.7 (C-1), 51.1 (CO_2*Me*), 60.7 (C-5), 106.8 (C-3), 114.1 (C-1′), 141.6 (C-2′), 149.8 (C-2), 171.9 (*C*O_2Me), 202.4 (CHO). Anal. Calcd for $C_{25}H_{46}O_5Si_2$: C, 62.19; H, 9.60. Found: C, 61.95; H, 9.78.

General Procedure C for Asymmetric [3 + 4] Annulation Using 23a,h,i and Homochiral 44: Reaction of 23a with Sodium Enolate of (−)-44. To a cooled (−80 °C) solution of NaHMDS (0.86 M in THF, 526 μL, 0.452 mmol) in THF (378 μL) was added dropwise a solution of (−)-44 (102 mg, 0.452 mmol) in THF (900 μL), and then the solution was stirred at the same temperature for 25 min. To this solution was added dropwise a cooled (−80 °C) solution of **23a** (80 mg, 0.377 mmol) in THF (5.7 mL) over a period of 9 min, and the mixture was stirred at the same temperature for 3 h. Then, the reaction mixture was poured into 10% aqueous NH_4Cl solution (15 mL), phases were separated, and the aqueous phase was extracted with Et_2O (5 mL × 2). Combined organic phases were washed with saturated brine (20 mL), dried, and concentrated. The residual oil was subjected to column chromatography (florisil, 5 g, elution with hexane/Et_2O = 6:1) to give **20a** (71 mg, 43%, $[\alpha]^{26}_D$ +15.9 (*c* 1.3, $CHCl_3$)) and **41a** (26 mg, 16%, **41a** (more polar)/**41a** (less polar) = 2.2). The optical purity of **20a** was determined to be 33% ee using a Daicel Chiralcel OD−H column (4.6 mm × 250 mm): eluent hexane, flow rate 0.5 mL/min, UV detection at 205 nm, t_R = 16.5 min (minor), 17.8 min (major).

Reaction of 23j with sodium enolate of (−)-44. Following general procedure B, sodium enolate of (−)-**44** (120 mg, 0.528 mmol) in THF (1.0 mL) was treated with **23j** (120 mg, 0.587 mmol) in THF (9.4 mL) at −80 °C for 7 min to give (+)-**20j** (159 mg, 70%) and (−)-**43j** (19 mg, 8%) after column chromatography (florisil, 6 g, elution with hexane/Et_2O = 3:1). For separation of (+)-**20j** and (−)-**43j**, MPLC (elution with hexane/Et_2O/CH_2Cl_2 = 20:1:1) was used. (+)-**20j**: Colorless oil. R_f = 0.38 (hexane/Et_2O = 4:1). IR (film) 1712, 1653, 1256 cm^{-1}. ^1H NMR (500 MHz) δ 0.11 (6H, s, Si*Me*$_2$Bu^t), 0.46 and 0.47 (each 3H, s, Si*Me*$_2$Ph), 0.87 (3H, d, J = 6.2 Hz, Me), 0.91 (9H, s, *t*-Bu), 2.26−2.40 (3H, m, H-6 and H-7), 2.75−2.81(1H, m, H-5), 2.84 (1H, d, J = 16.7 Hz, H-2), 3.56 (1H, d, J = 16.7 Hz, H-2), 4.81 (1H, dd, J = 6.4, 2.1 Hz, H-4), 4.86 (1H, dd, J = 11.9, 8.5 Hz, H-1′), 6.13 (1H, d, J = 11.9 Hz, H-2′), 7.35−7.44 (3H, m, Ph), 7.54−7.60 (2H, m, Ph). ^{13}C NMR (125 MHz) δ −5.1 (Si*Me*$_2$Bu^t), −1.1 (Si*Me*$_2$Ph), 18.0 (Me), 18.5 (*C*Me$_3$), 25.9 (C*Me*$_3$), 35.9 (C-6), 39.5 (C-5), 48.5 (C-7), 50.0 (C-2), 110.5 (C-1′), 111.5 (C-4), 128.1, 130.1, 133.5, 137.2 (Ph), 142.1 (C-2′), 145.1 (C-3), 207.9 (C-1). HRMS calcd for $C_{24}H_{38}O_3Si_2$ 430.2359, found 430.2360. $[\alpha]^{27}_D$ +3.0 (*c* 1.0, $CHCl_3$). The optical purity was determined to be 11% ee using a Daicel Chiralcel OD−H column (4.6 mm × 250 mm): eluent hexane/*i*-PrOH = 200:1, flow rate 1.0 mL/min, UV detection at 205 nm, t_R = 6.4 min (major), 7.2 min (minor). (−)-**43j**: Colorless oil. R_f = 0.30 (hexane/Et_2O = 5:1). IR (film) 1711, 1657, 1256 cm^{-1}. ^1H NMR (500 MHz) δ 0.12 (6H, s, Si*Me*$_2$Bu^t), 0.47 and 0.49 (each 3H, s, Si*Me*$_2$Ph), 0.84 (3H, d, J = 6.9 Hz, Me), 0.91 (9H, s, *t*-Bu), 2.28−2.35 (1H, m, H-7), 2.35−2.42 (1H, m, H-6), 2.49−2.57 (2H, m, H-5 and H-7), 2.82 (1H, d, J = 18.1 Hz, H-2), 3.41 (1H, d, J = 18.1 Hz, H-2), 4.66 (1H, dd, J = 6.6, 2.3 Hz, H-4), 4.75 (1H, dd, J = 11.9, 9.6 Hz, H-1′), 6.20 (1H, d, J = 11.9 Hz, H-2′), 7.36−7.44 (3H, m, Ph), 7.56−7.61 (2H, m, Ph). ^{13}C NMR (125 MHz) δ −5.0 (Si*Me*$_2$Bu^t), −1.1 and −1.0 (Si*Me*$_2$Ph), 18.6 (*C*Me), 18.8 (Me), 25.9 (C*Me*$_3$), 33.2 (C-6), 43.8 (C-5), 48.4 (C-7), 50.8 (C-2), 111.2 (C-1′), 112.6 (C-4), 128.2, 130.2, 133.6, 137.1 (Ph), 141.7 (C-2′), 146.6 (C-3), 208.8 (C-1). HRMS calcd for $C_{24}H_{38}O_3Si_2$ 430.2359, found 430.2357. The stereochemistries at C-5 and C-6 were assigned on the basis of the observed correlation between the hydrogens at C-2′ and Me in NOESY experiments. $[\alpha]^{27}_D$ −5.1 (*c* 0.17, $CHCl_3$). The optical purity was determined to be 15% ee using a Daicel Daicel Chiralcel OD−H column (4.6 mm × 250 mm): eluent hexane/*i*-PrOH = 200:1, flow rate 1.0 mL/min, UV detection at 205 nm, t_R = 6.4 min (minor), 7.4 min (major).

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Supporting Information Available: Experimental details and spectral data not reported in the Experimental Section and X-ray structural data for compound (+)-**53**. This material is available free of charge via the Internet at http://pubs.acs.org.

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